AMENDMENT

Please amend claim 1 and cancel claim 17 as follows.

1. (Currently amended) A method of ~~suppressing, reducing, delaying, or ameliorating a symptom of multiple sclerosis associated with an IL-10 deficiency or increased~~ decreasing an IFN-γ parameter in a subject having an excess of IFN-γ, the method comprising:

(a) evaluating the IFN-γ parameter of a subject;

(b) comparing the IFN-γ parameter in the subject to the IFN-γ parameter of a normal subject, wherein a substantial increase in the IFN-γ parameter in the subject relative to the normal subject indicates that the subject has the excess IFN-γ; and

(c) administering to the subject having the excess IFN-γ an agonist of an interleukin-21 (IL-21)/IL-21 receptor (IL-21R) ~~in an amount sufficient to suppress, reduce, delay, or ameliorate the symptom of multiple sclerosis associated with an IL-10 deficiency or increased IFN-γ~~, wherein said agonist is selected from the group consisting of:

(i) a human IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2,

(ii) a murine IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:4,

(iii) an agonistic anti-human IL-21R antibody, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:6, and

(iv) an agonistic anti-murine IL-21R, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least 95% identical to the

amino acid sequence of SEQ ID NO:8, ~~an antigen-binding fragment of an agonistic anti-human IL-21R antibody, and an antigen-binding fragment of an agonistic anti-murine IL-21R antibody~~ wherein the IFN-γ parameter of the subject having the excess IFN-γ is decreased at least 2 fold.

2-3. (Canceled)

4. (Currently amended) The method of claim ~~[[1]]~~ 9, wherein the agonist is a human IL-21 polypeptide that comprises the amino acid sequence of SEQ ID NO:2.

5. (Currently amended) The method of claim 1, wherein the agonist is an agonistic anti-human IL-21R antibody or an antigen-binding fragment thereof capable of binding to an IL-21R comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:6.

6. (Previously presented) The method of claim 5, wherein the agonistic anti-human IL-21R antibody or the antigen binding fragment thereof is a humanized antibody or an antigen binding fragment thereof.

7. (Original) The method of claim 1, further comprising administering to the subject at least one anti-inflammatory agent.

8. (Previously presented) The method of claim 7, wherein the anti-inflammatory agent is selected from the group consisting of IFNβ-1α and IFNβ-1β.

9. (Currently amended) The method of claim 1, wherein the subject is a ~~mammal~~ human, and the agonist is a human IL-21 polypeptide that comprises a sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2 and is capable of binding to a human IL-21R.

10. (Original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered in the form of a single dose.

11. (Original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered as a series of doses separated by intervals of days, weeks or months.

12. (Original) The method of claim 1, wherein the IL-21/IL-21R agonist is administered by injection.

13. (Original) The method of claim 12, wherein the IL-21/IL-21R agonist is injected into the central nervous system.

14. (Previously presented) The method of claim 12, wherein the IL-21/IL-21R agonist is injected intrathecally or intravenously.

15. (Original) The method of claim 12, wherein the IL-21/IL-21R agonist is injected into the lumbar cerebrospinal fluid.

16-18. (Canceled)

19. (Currently amended) The method of claim 1, further comprising, after the administering, evaluating ~~an IL-10~~ the IFN-γ parameter of the subject.

20-28. (Canceled)

29. (Currently amended) A method of ~~suppressing, reducing, delaying, or ameliorating multiple sclerosis associated with an IL-10 deficiency or increased~~ decreasing an IFN-γ parameter in a ~~mammalian~~ subject having an excess of IFN-γ, the method comprising:

(a) evaluating the IFN-γ parameter of a subject;

(b) comparing the IFN-γ parameter in the subject to the IFN-γ parameter of a normal subject, wherein a substantial increase in the IFN-γ parameter in the subject relative to the normal subject indicates that the subject has the excess IFN-γ; and

(c) administering to the subject having the excess IFN-γ an agonistic interleukin-21 (IL-21) polypeptide, wherein the agonistic IL-21 polypeptide is a human IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2 or a murine IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:4, ~~in an amount sufficient to suppress, reduce, delay, or ameliorate multiple sclerosis associated with an IL-10 deficiency or increased IFN-γ or at least~~

~~one symptom of multiple sclerosis associated with an IL-10 deficiency or increased IFN-γ, in~~ wherein the IFN-γ parameter of the subject having the excess IFN-γ is decreased at least 2 fold.

30. (Currently amended) The method of claim 29 wherein the subject is human, and the agonistic IL-21 polypeptide is a human IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2 .

31. (Previously presented) The method of claim 30 wherein the human IL-21 polypeptide comprises SEQ ID NO:2.

32. (Previously presented) The method of claim 30 wherein the human IL-21 polypeptide is recombinantly produced.

33. (Previously presented) The method of claim 32 wherein the human IL-21 polypeptide is recombinantly produced in a bacterial cell.

34. (Currently amended) A method of ~~suppressing, reducing, delaying, or ameliorating an IL-10 deficiency, or a disorder associated with~~ increasing an IL-10 parameter ~~deficiency~~ in a ~~mammalian~~ subject having an IL-10 deficiency, the method comprising:

(a) evaluating the IL-10 parameter of a subject;

(b) comparing the IL-10 parameter in the subject to the IL-10 parameter of a normal subject, wherein a substantial decrease in the IL-10 parameter in the subject relative to the normal subject indicates that the subject has an IL-10 deficiency; and

(c) administering to the subject having an IL-10 deficiency an agonistic interleukin-21 (IL-21) polypeptide, wherein the agonistic IL-21 polypeptide is a human IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2 or a murine IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:4, wherein the IL-10 parameter of the subject having the IL-10 deficiency is increased at least 1.2 fold ~~in an amount sufficient to increase IL-10 expression in the subject~~.

35. (Currently amended) A method of ~~suppressing, reducing, delaying, or ameliorating an immunological disorder associated with~~ increasing an IL-10 parameter ~~deficiency~~ in a ~~mammalian~~ subject having an IL-10 deficiency, the method comprising:

(a) evaluating ~~an~~ the IL-10 parameter in a ~~mammalian~~ subject;

(b) comparing the IL-10 parameter in the ~~mammalian~~ subject to ~~an~~ the IL-10 parameter in a normal ~~mammalian~~ subject ~~known not to have an immunological disorder associated with an IL-10 deficiency~~, wherein a substantial decrease in the IL-10 parameter in the ~~mammalian~~ subject relative to the normal ~~mammalian~~ subject indicates that the ~~mammalian~~ subject ~~requires suppression, reduction, delay, or amelioration of an immunological disorder associated with~~ has an IL-10 deficiency; and

(c) administering[[,]] to the ~~mammalian~~ subject having an IL-10 deficiency [[,]] an ~~agonistic~~ agonist of an interleukin-21 (IL-21)/IL-21 receptor (IL-21R) ~~polypeptide~~, wherein ~~agonistic IL-21 polypeptide is~~ the agonist is selected from the group consisting of:

(i) a human IL-21 polypeptide ~~or~~ comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2,

(ii) a murine IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:4,

(iii) an agonistic anti-human IL-21R antibody, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:6, and

(iv) an agonistic anti-murine IL-21R, or an antigen-binding fragment thereof, capable of binding to an IL-21R comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:8,

wherein the IL-10 parameter of the subject having the IL-10 deficiency is increased at least 1.2 fold~~, in an amount that is dependent on the results of comparing step (b)~~.

36. (Original) The method of claim 35 wherein the IL-10 parameter comprises quantitative information about levels of IL-10 protein or IL-10 mRNA.

37-49. (Canceled)

50. (New) The method of claim 1 wherein the IFN-γ parameter comprises quantitative information about levels of IFN-γ protein or IFN-γ mRNA.

51. (New) The method of claim 9 wherein the human IL-21 polypeptide is recombinantly produced.

52. (New) The method of claim 51 wherein the human IL-21 polypeptide is recombinantly produced in a bacterial cell.

53. (New) The method of claim 29 wherein the IFN-γ parameter comprises quantitative information about levels of IFN-γ protein or IFN-γ mRNA.

54. (New) The method of claim 34 wherein the subject is human, and the agonistic IL-21 polypeptide is a human IL-21 polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2 .

55. (New) The method of claim 54 wherein the human IL-21 polypeptide comprises SEQ ID NO:2.

56. (New) The method of claim 54 wherein the human IL-21 polypeptide is recombinantly produced.

57. (New) The method of claim 56 wherein the human IL-21 polypeptide is recombinantly produced in a bacterial cell.

58. (Original) The method of claim 34 wherein the IL-10 parameter comprises quantitative information about levels of IL-10 protein or IL-10 mRNA.

59. (New) The method of claim 35, wherein the subject is a human and the agonist is a human IL-21 polypeptide that comprises a sequence at least 95% identical to the amino acid sequence of SEQ ID NO:2 and is capable of binding to a human IL-21R.

60. (New) The method of claim 59 wherein the agonist is a human IL-21 polypeptide that comprises the amino acid sequence of SEQ ID NO:2.

61. (New) The method of claim 60 wherein the human IL-21 polypeptide is recombinantly produced.

62. (New) The method of claim 61 wherein the human IL-21 polypeptide is recombinantly produced in a bacterial cell.

63. (New) The method of claim 35, wherein the agonist is an agonistic anti-human IL-21R antibody or an antigen-binding fragment thereof capable of binding to an IL-21R comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO:6.

64. (New) The method of claim 63, wherein the agonistic anti-human IL-21R antibody or the antigen binding fragment thereof is a humanized antibody or an antigen binding fragment thereof.

65. (New) The method of claim 35, further comprising administering to the subject at least one anti-inflammatory agent.

66. (New) The method of claim 65, wherein the anti-inflammatory agent is selected from the group consisting of IFNβ-1α and IFNβ-1β.

67. (New) The method of claim 35, wherein the IL-21/IL-21R agonist is administered in the form of a single dose.

68. (New) The method of claim 35, wherein the IL-21/IL-21R agonist is administered as a series of doses separated by intervals of days, weeks or months.

69. (New) The method of claim 35, wherein the IL-21/IL-21R agonist is administered by injection.

70. (New) The method of claim 69, wherein the IL-21/IL-21R agonist is injected into the central nervous system.

71. (New) The method of claim 69, wherein the IL-21/IL-21R agonist is injected intrathecally or intravenously.

72. (New) The method of claim 69, wherein the IL-21/IL-21R agonist is injected into the lumbar cerebrospinal fluid.

73. (New) The method of claim 35, further comprising, after the administering, evaluating the IL-10 parameter of the subject.